REMARKS

Claims 1-10 and 13 are currently pending. Claim 13 has been amended. The amendment to claim 13 does not constitute new matter.

The Examiner has rejected claim 13 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner has rejected claims 1-9 under 35 U.S.C. § 102(b) as anticipated by U.S. Patent No. 5,165,938 ("Knighton"). The Examiner has rejected claims 1-4 and 6-9 under 35 U.S.C. § 102(b) as anticipated by U.S. Patent No. 5,185,160 ("Chao"). The Examiner has rejected claims 1-10 and 13 under 35 U.S.C. § 103(a) as obvious over Knighton in view of Chao, taken with U.S. Patent No. 5,697,980 ("Otani") and Zeng, Southeast Asian Journal of Tropical Medicine and Public Health, 1993, vol. 24, supp. 1, pages 204-205 ("Zeng").

For the reasons detailed below, the rejections should be withdrawn and the claims allowed to issue. Entry of the foregoing amendments is respectfully requested.

The Claims Are Supported By The Specification

The Examiner has rejected claim 13 as failing to comply with the written description requirement, stating that the term "polyactin" has no support in the written description.

Applicants note that claim 13 and the specification have been amended to recite "polyactone" instead of "polyactin." Applicants submit that polyactone is a intramolecular polymer, and that a person of ordinary skill in the art would recognize that the term "polyacton," as originally recited in the specification, is an obvious misspelling of the term "polyactone." As further evidence, Applicants note that the German priority document recites "polyaktone."

Accordingly, Applicants submit that the amendment to the claims and the specification do not present new matter, and respectfully request that the amendments be entered and the rejection be withdrawn.

The Claims Are Novel

The Examiner has rejected claims 1-9 under 35 U.S.C. § 102(b) as anticipated by U.S. Patent No. 5,165,938 ("Knighton"). The Examiner states that due to product-by-process limitations in the claim, only the structure implied by the steps are limiting, and that the "final structure of the presently claimed product encompasses a sterile drug product that would be free of viruses." The Examiner further states that Knighton "teaches that starting materials that might have potential contamination with hepatitis are avoided."

Applicants disagree with the Examiner's reading of Knighton. Applicants note that the Examiner is effectively arguing that the Knighton is inherently virus-free, as Knighton does not explicitly teach virus depletion or inactivation. To show that a limitation is inherent in a reference, the Examiner must "provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." MPEP § 2112 (emphasis in original). Therefore, to inherently anticipate, the allegedly inherent limitation must: 1) necessarily be present in the reference, as opposed to possibly present; 2) always be present; and 3) be recognized as necessarily present by a person of ordinary skill in the art. See *Crown Operations International, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1374 (Fed. Cir. 2002).

Applicants assert that the platelet-rich preparations of Knighton are not necessarily virus-free, and will not always be virus-free. The passage cited by the Examiner states:

> "Utilization of blood from the injured individual to be treated is especially preferred since it avoids exposure to possible hepatitis or other contaminants from banked blood. The use of a patient's own blood would also eliminate any possible allergic reactions."

Knighton at col. 4, lines 54-61. As previously noted, Knighton does not provide any teaching or suggestion regarding virus depletion or inactivation. Applicants assert that this passage merely describes the use of autologous serum to avoid allergic reactions and infections with viruses not already present in the individual. Because Knighton does not teach a virus depletion or inactivation step, any viruses which are already present will remain in the platelet-rich plasma preparations of Knighton; therefore, the platelet-rich preparations of Knighton are not necessarily virus-free. Furthermore, Knighton teaches the use of allogeneic sources of blood to produce the platelet-rich preparations; absent a virus depletion or inactivation step, these preparations will not necessarily be virus-free. Accordingly, Knighton cannot inherently anticipate the present invention.

The Examiner has rejected claims 1-4 and 6-9 under 35 U.S.C. § 102(b) as anticipated by U.S. Patent No. 5,185,160 ("Chao"). The Examiner states that "Applicants' definitions of 'microparticles' in the as-filed specification are rather vague," and further states that the microparticles of Chao fall within the definition of microparticles as defined in Horstman et al., Crit Rev Oncol Hematol, 1999, 30(2):111-42 ("Horstman") (already of record).

Applicants submit that, at the time of filing the present application, a person of ordinary skill in the art would recognize that the term "microparticle" carried a specific meaning. Microparticles are submicron fragments shed from the plasma membrane of live, viable cells which have been stimulated. See Horstman at page 113, left column. Originally referred to as 'platelet dust', it is known that platelets, once activated, release microparticles, which are heterogenic in size. Wolf, Br J Haematol 1967;13:269-288 (attached as Exhibit 1). For example, in platelets, microparticle release may be stimulated by epinephrine, adenosine

diphosphate, thrombin, collagen, Ca2+ ionophore A23187, complement complex C5b-9, and/or antiplatelet antibodies. See Horstman at pages 119-123; Wiedmer *et al.*, Blood, 1991, 78(11):2880-2886 (attached as Exhibit 2). Thus, it is important to recognize that microparticle shedding is a controlled process induced by cell activation. See Horstman at page 113 (Microparticles are "known to be a normal consequence of platelet activation."). For example, it has been shown that a controlled reaction involving transverse migration of anionic phospholipids such as phosphatidylserine and phosphatidylethanolamine from the inner layer to the outer layer of the plasma membrane is involved in the release of microparticles. Zwaal *et al.*, Blood, 1997, 89(4):1121-1132, at page 1122 (Figure 1) and 1123, right column (attached as Exhibit 3). Shear stress, without cell disintegration, is a mechanical factor inducing microparticle release in platelets and other cell types. George et al., Transfusion 1988;28:123-126 (attached as Exhibit 4).

More recent publications also stress that microparticles are the product of a controlled shedding process. For example, Simak *et al.*, Transfusion Medicine Reviews, 2006, 20(1):1-26, at page 2 (attached as Exhibit 5) state:

> "It is important to note that [microparticle] release is not a random process such as the degradation of the plasma membrane of dying necrotic cells but a highly controlled process associated with different types of cell stimulation."

Thus, more recent research and publications support what was known at the time of filing of the present application: the release of microparticles is a controlled process associated with the activation of cells.

In contrast, Chao discloses washed platelets which are resuspended in physiologic saline; in other words, the platelets utilized in Chao are not activated. See Chao at col. 4, lines 6-16. The resuspended platelets are disrupted by repeated freezing and thawing or by osmotic pressure. See Chao at col. 4, lines 17-27. Both processes result in cell disintegration, thereby producing a

suspension of cytoplasmic components and platelet membranes, the latter termed platelet ghosts in Chao. See Chao at col. 4, lines 21-24. Following heat treatment, the platelet ghosts are subjected to sonication, resulting in the platelet membrane vesicles which Chao refers to as microparticles. See Chao at col. 4, lines 46-56. Furthermore, as noted above, the state of the art at the time of filing acknowledges that microparticles are exclusively released from live cells by a controlled mechanism. As such, Chao does not disclose the controlled shedding process associated with microparticles as described above, and the platelet ghosts of Chao are derived from the ruptured plasma membranes of dead cells. Accordingly, the "microparticles" created by Chao will be distinct from the microparticles of the present invention. Thus, a person of ordinary skill in the art would understand that the term "microparticle" was not correctly used by Chao, and the microparticles of Chao are distinct from the microparticles of the present invention.

Based upon the foregoing, Applicants assert that the microparticles as described Chao are not the same as the microparticles of the present invention. Accordingly, Applicants respectfully request that the rejection be withdrawn.

The Claims Are Not Obvious

The Examiner has rejected claims 1-10 and 13 under 35 U.S.C. § 103(a) as obvious over Knighton in view of Chao, taken with U.S. Patent No. 5,697,980 ("Otani") and Zeng, Southeast Asian Journal of Tropical Medicine and Public Health, 1993, vol. 24, supp. 1, pages 204-205 ("Zeng").

Applicants disagree with the Examiner, and submit that the Examiner has not set forth a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, the Examiner must meet three criteria. The Examiner must establish that (1) there is some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there is a reasonable expectation of success; and (3) the prior art reference (or references when combined) teach or suggest all the claim limitations. See MPEP §§ 706.02(j) and 2143. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q2d 1438 (Fed. Cir. 1991).

There is no suggestion or motivation to combine these references. As noted above, the microparticles of Chao are platelet membrane fragments derived from disruption of the platelet membranes, and thus are not the same as the microparticles of Knighton. A person of ordinary skill in the art would not be motivated to combine Knighton and Chao, as the microparticles of the two references are different from one another. In fact, Chao teaches away from the present invention, because Chao subjects the platelets to both heat treatment and sonication, both of which can result in disruption of the plasma membrane of the platelet cells. As discussed above,

the present invention utilizes microparticles which are released from activated platelets through a controlled shedding process, and do not involve disruption of the plasma membrane.

Furthermore, Otani does not make any reference to the use of the disclosed artificial filling and prosthetic material in conjunction with agents that promote wound healing or tissue regeneration. Similarly, Knighton and Chao do not make any reference to the use of microparticles in an artificial filling and prosthetic material. Thus, there is no suggestion or motivation to combine the references to reach the present invention. Applicants submit that the Examiner is making a determination of obviousness based upon impermissible hindsight, because the references do not provide an "objective reason to combine the teachings of the references." MPEP 2143.01 ("The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination.") (emphasis in original).

With regard to Zeng, Applicants note that claim 13 and the specification have been amended to recite "polyactone" instead of "polyactin." Accordingly, Applicants submit that the reference to Zeng has been obviated.

Applicants submit that a person of ordinary skill in the art would not have a reasonable expectation of success in combining the cited references to reach the present invention. As noted above, the microparticles of Chao and Knighton are different, and are prepared by different processes. The process by which the microparticles of Chao are prepared results in disruption of the plasma membrane, and loss of cytoplasm. As such, the combination of Knighton and Chao would not result in the microparticles disclosed in the present invention, as discussed in greater detail above. Furthermore, there is no teaching or guidance in any of the cited references with regard to the combination of the microparticles in an organic polymer. A person of ordinary skill

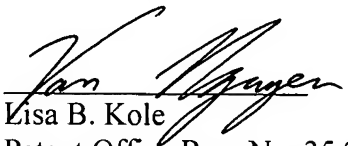
in the art could not reasonably expect to succeed in such a combination based upon the teachings of the references cited by the Examiner, as the references do not provide any teaching or guidance regarding this combination.

Based upon the foregoing, Applicants submit that the present invention is not obvious in over Knighton and Chao in view of Otani, and respectfully request withdrawal of the rejections.

CONCLUSION

Entry of the foregoing amendments and remarks into the file of the above-identified application is respectfully requested. Applicants believe that the invention described and defined by claims 1-10 and 13 are patentable over the rejections of the Examiner. Withdrawal of all rejections and reconsideration of the amended claims is requested. Allowance is earnestly sought.

Respectfully submitted,



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